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Novel base-initiated reactions of *N*-substituted pyridinium salts [1]

Teruo Umemoto [a,*,2], Ginjiro Tomizawa [a,1], Hitoharu Hachisuka [b,*], Masakatsu Kitano [b]

[a] *Sagami Chemical Research Center, Nishi-Ohnuma 4-4-1, Sagamihara, Kanagawa 229, Japan*

[b] *Chemical Division, Daikin Industries, Ltd., Nishi-Hitotsuya 1-1, Settsu, Osaka 566, Japan*

Abstract

Reaction of *N*-fluoropyridinium triflate with a base in dichloromethane gave 2-chloropyridine as the major product along with 2-pyridyl triflate and 2-fluoropyridine, regardless of the nature of the base. This base-initiated reaction was also shown to take place similarly in other halogenated alkanes, ethers, a nitrile, aromatics, a ketone, vinyl ethers, alcohols and trimethylsilyl acetate as solvents to give pyridine derivatives substituted with a solvent molecule(s) at the 2-position. *N*-(Trifluoromethanesulfonyloxy)- and (benzenesulfonyloxy)pyridinium salts were found to undergo the same base-initiated reaction. These reactions may be explained by a postulated singlet carbene (canonical formula **11b**) produced through proton abstraction of *N*-substituted pyridinium salts. A similar carbene reaction may thus likely occur in the thermal decomposition of thiatriazole **10**. *Ab initio* MO calculations revealed the structure and properties of the labile deprotonated *N*-fluoropyridinium cation and supported the carbene intermediate reaction mechanism rather than a pyridynium or pyridyl cation mechanism. Quarroz's reports on the reactions of picolinic acid *N*-oxide and the reported reactions of pyridines with F_2, CH_3COOF or $CsSO_4F$ in solvents may be explained by this carbene mechanism.

Keywords: Base-initiated reactions; *N*-fluoropyridinium salts; *Ab initio* MO calculations; Reaction mechanism; NMR spectroscopy; IR spectroscopy; Mass spectrometry

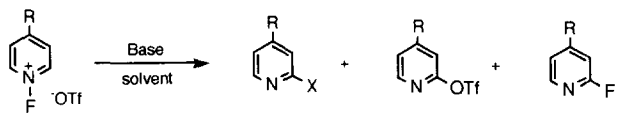
1. Introduction

Reactions of pyridines, pyridine *N*-oxides or pyridinium salts with bases have been studied in detail and the results have shown addition, addition–elimination, elimination–addition, ring-opening and proton-abstraction followed by nucleophilic reaction which occur depending on the nature of the pyridine rings and bases [2]. The authors reported a new type of base-induced reaction of *N*-fluoropyridinium salts in a preliminary communication [3]. Treatment with a nitrogen- or oxygen-base in a solvent afforded a 2-substituted pyridine derivative(s) produced through reaction with a normally unreactive solvent molecule(s). In the absence of solvent, *N*-fluoropyridinium tetrafluoroborates, hexafluorophosphates and hexafluoroantimonates afforded 2-fluoropyridines in good yield [4]. *N*-Fluoropyridinium salts function as fluorinating agents toward carbon-bases to give C–F compounds [5]. This paper describes novel base-initiated reactions of *N*-fluoropyridinium salts and other *N*-substituted pyridinium salts, *ab initio* MO calculations on deprotonated *N*-fluoropyridinium cation and related reactive species, and a possible reaction mechanism based on the present reaction data and MO calculations.

2. Results

2.1. Base-initiated reactions of N-fluoropyridinium salts with various kinds of bases and solvents (see Scheme 1)

N-Fluoropyridinium triflate (**1**) in dichloromethane was reacted with various bases at room temperature and the results obtained are shown in Table 1. The major product was 2-chloropyridine (**3a**) along with 2-pyridyl triflate (**5**) and 2-fluoropyridine (**7**) as minor products, regardless of the nature of nitrogen and oxygen bases used. A fluoride anion base also gave the same products but with a slight increase in **7** (Run



1 (R=H) **2** (R=*t*-Bu) **3** (R=H) **4** (R=*t*-Bu) **5** (R=H) **6** (R=*t*-Bu) **7** (R=H) **8** (R=*t*-Bu)

Scheme 1.

* Corresponding authors.

[1] See ref. [1].

[2] Present address: MEC Laboratory, Daikin Industries, Ltd., Miyukigaoka 3, Tsukuba, Ibaraki 305, Japan.

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Table 1
Base-initiated reactions of *N*-fluoropyridinium triflate (**1**) in dichloromethane

Run No.	Base [a]	Time	Yield (%) [b]		
			3a(X=Cl)	**5**	**7**
1	Et_3N	5 min	62	21	5
2 [c]	Et_2NH	5 min	63	22	6
3	$^iPr_2NEt$	5 min	60	16	5
4	pyridine	60 min	41	23	5
5	2,6-di-t-butylpyridine	2 d	68	3	9
6 [d]	MeONa	10 min	25	7	5
7	^{t}BuOK	10 min	35	5	7
8	$PhCH_2N^+Me_3^-OH$	3 h	34	3	6
9 [e]	CH_3COONa	2 d	40	3	2
10	CH_3COONa (2 equiv.)	4 d	63	3	8
11	$^nBu_4N^+F^-$	5 min	28	4	14

[a] An equivalent amount of base to **1** was used, unless otherwise noted.
[b] Determined by GLC.
[c] 2-(Diethylamino)pyridine (**3p**) was detected in 1% yield.
[d] 2-(Methoxy)pyridine (**3d**) was detected in 9% yield.
[e] This reaction was not completed.

11). Reactions with di- and tri-ethylamine and ethyldi(isopropyl)amine were vigorously exothermic, proceeding rapidly to completion (<5 min). The reaction with pyridine was rather slow (1 h) and quite slow with 2,6-di-*t*-butylpyridine (2 d). Salt **1** was either slightly or not substituted at all by bases at the 2- or 4-position of the pyridine ring. In Runs 2 and 6, the base-coupling products, 2-(diethylamino)pyridine (**3p**) and 2-methoxypyridine (**3d**) were formed in 1% and 9% yield, respectively. Even when using diethylamine as the solvent, **3p** could not be detected; the products formed were **5** (61%) and **7** (18%).

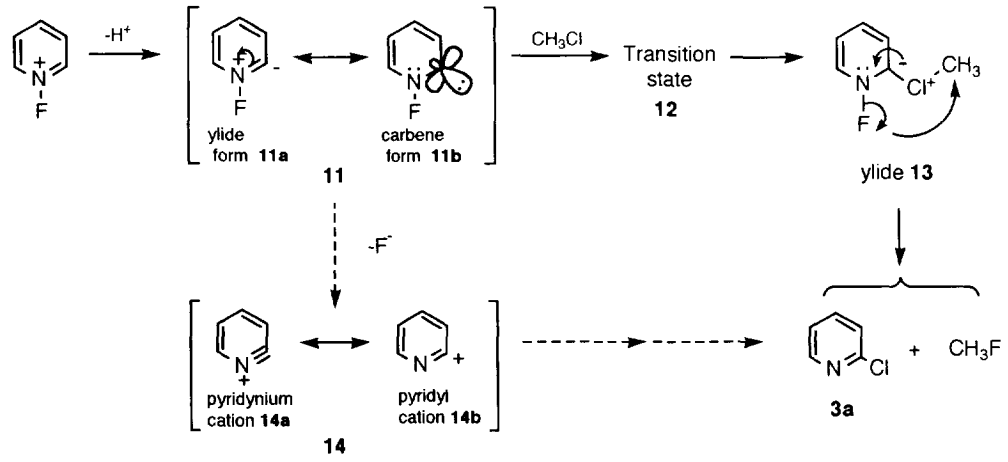
Table 2 shows the results of the triethylamine base-initiated reactions of *N*-fluoropyridinium salts **1** and **2** in various solvents at room temperature. In a series of dihalomethane solvents, **3a** and 2-bromopyridine (**3b**) were each formed in about 60% yield, while 2-iodopyridine (**3c**) was produced in only a trace amount whereas the yields of **5** and **7** were noted to increase greatly. Benzotrichloride gave **3a** (11%), no 2-arylpyridines, **5** (58%) and **7** (20%). GC-MS analysis indicated that the reaction mixture contained a small amount of (dichlorofluoromethyl)benzene. Methanol, trimethylsilyl acetate, tetrahydrofuran (THF), dioxan and acetone afforded the 2-oxygenated pyridine derivatives **3d–j** along with **5** and **7**. Product **3g** resulted from a combination of two molecules of THF. With 2,3-dimethyl-2-butene and tetrachloroethylene, solvent-substituted pyridines could not be detected and only **5** or **6** and **7** or **8** were formed in total yields of about 80%.

Tetrachloroethylene failed to give rise to chloropyridine **3a**, while fluoropyridine **7** was formed extensively in addition to **5**. Vinyl ethyl ether and 2,3-dihydrofuran gave the oxygen-substituted pyridines **4** and **3k**, but no carbon-substituted pyridines could be found. Benzene and furan gave the carbon-substituted pyridines **3m–o**. With furan, a 1.3:1 mixture of 2-(2′- and 3′-furyl)pyridines (**3n**) and (**3o**) was obtained.

Table 2
Triethylamine-initiated reactions of *N*-fluoropyridinium salts in various solvents

Run No. [a]	Salt	Solvent	Yield (%) [b]		
			3 or **4**	**5** or **6**	**7** or **8**
1	**1**	CH_2Br_2	60 **3b** (X=Br)	27	4
2	**1**	CH_2I_2	3 **3c** (X=I)	48	17
3 [c]	**1**	$PhCCl_3$	11 **3a** (X=Cl)	58	20
4	**1**	MeOH	79 **3d** (X=OMe)	4	2
5	**1**	MeOH/NaOTf [d]	64 **3d** (X=OMe)	22	3
6	**1**	$CH_3COOSiMe_3$	34 **3e** ($X=OCOCH_3$)	43	9
7	**1**	THF	25 **3f** [$X=O(CH_2)_4F$]	33	6
			5 **3g** [$X=O(CH_2)_4O(CH_2)_4F$]		
8	**1**	Dioxan	15 **3h** [$X=O(CH_2)_2O(CH_2)_2F$]	36	6
9	**1**	Acetone	25 **3i** ($X=OCFMe_2$)	14	5
			25 **3j** ($X=OCMe=CH_2$)		
10	**2**	$CH_2=CHOEt$	12 **4** ($X=OCH=CH_2$)	45	14
11	**1**	2,3-Dihydrofuran	9 **3k** [$X=OCH=CH(CH_2)_2F$] [e]	24	7
12	**1**	CH_3CN	55 **3l** ($X=NHCOCH_3$)	7	3
13	**2**	$Me_2C=CMe_2$	Not detected	58	24
14	**1**	$Cl_2C=CCl_2$	Not detected	43	35
15	**1**	Benzene	33 **3m** (X=Ph)	42	15
16	**1**	Furan	17 **3n** (X=2-Furyl)	39	9
			13 **3o** (X=3-Furyl)		

[a] An equivalent amount of triethylamine to **1** or **2** was used.
[b] Determined by GC except for **3c**, **3g**, **3l**, **3m**, **3n** and **3o** which were isolated yields.
[c] GC-MS analysis indicated $PhCCl_2F$ as being produced in this reaction.
[d] This reaction was carried out in the presence of 2 equiv. of sodium triflate as an additive in methanol.
[e] **3k** is a *cis* isomer.



Scheme 2. Reaction model for calculation.

Acetonitrile gave the nitrogen-substituted pyridine **3l** in 55% yield.

2.2. Base-initiated reactions of other N-substituted pyridinium salts

N-(Trifluoromethanesulfonyloxy)pyridinium triflate (**9**), derived in situ from pyridine *N*-oxide and triflic anhydride in dichloromethane, was treated with an equivalent amount of triethylamine at room temperature. An exothermic reaction occurred immediately to give **3a** and **5** in 29% and 34% yield, respectively. Salt **9** prepared as above was isolated and treated with diethylamine solvent at room temperature to give **5** (21%) and the base-coupling product, **3p** (12%). Treatment of pyridine *N*-oxide and benzenesulfonyl chloride in dichloromethane with triethylamine at room temperature provided **3a** and 2-pyridyl benzenesulfonate in 22% and 34% yield respectively. A mixture of pyridine *N*-oxide and acetic anhydride in dichloromethane failed to react with triethylamine at room temperature.

2.3. Reaction of picolinic acid with F_2 in acetonitrile

Picolinic acid was fluorinated with a 1:9 mixture of F_2 and N_2 gas in acetonitrile at -40°C, followed by acid hydrolysis. (Acetylamino)pyridine (**3l**) thus formed was isolated in 14% yield from the reaction mixture.

2.4. Thermal decomposition of 1,2,3,5-thiatriazolo-[5.4.a]pyridin-3-oxide (10) in methanol or 1,2-dichloroethane

A solution of thiatriazole **10** in methanol was heated under reflux for 12 h in the presence of 2 equiv. of sodium triflate to give **3d** and **5** in 34% and 16% yields, respectively. Heating a solution of **10** in 1,2-dichloroethane under reflux for 7 h resulted in **3a** in 17% yield.

2.5. Ab initio MO calculations

As shown in Scheme 2, the base-initiated reaction of the *N*-fluoropyridinium cation with chloromethane was postulated, and the structures and total energies of the *N*-fluoropyridinium cation, the deprotonated intermediate **11**, the transition state **12** and the ylide intermediate **13** were calculated by *ab initio* MO methods. These structures are shown in Fig. 1 and the total energies, bond distances, π-electron populations and Mulliken charges are summarized in Tables 3–6, respectively. Bond distances of triflate **1** obtained by X-ray crystallographical analysis [6] are also summarized as references in Table 4. Thus, the calculated

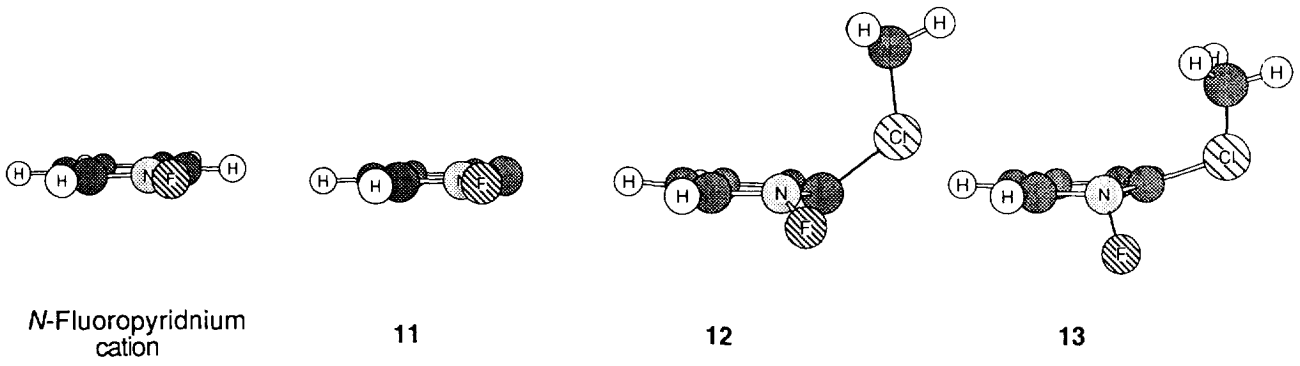


Fig. 1. Structures determined by RHF calculations.

Table 3
Total energies (RHF/DZ+P) [a]

Molecule	E_{total} (a.u.) [b]
N-Fluoropyridinium cation	−345.890 260 3
11	−345.472 251 6
12	−844.537 932 1
13	−844.570 662 9
14	−245.807 976 6
CH_3Cl	−499.095 059 0
F^-	−99.435 265 8 [c]

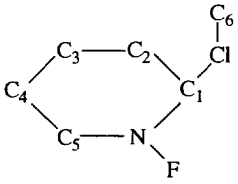
[a] The following basis set was used except for F^-; (11,7,1)/[6,4,1] for Cl, (9,5,1)/[3,2,1] for C and F, and (4,1)/[2,1] for H.
[b] 1 a.u. = 627 kcal mol^{-1}.
[c] Augmented with diffusion functions [$\zeta(s) = 0.004548$, $\zeta(p) = 0.034$].

bond distances of the *N*-fluoropyridinium cation are close to the observed ones of **1**. Another possible mechanism [7] via the pyridynium or pyridyl cation **14** was also examined and the total energies of **14** and F^- were calculated (Table 3).

According to the results of these calculations, the structure of deprotonated intermediate **11** lies between two canonical formulas, the ylide form **11a** and the carbene form **11b**. Thus, while all the C–C bond distances in the *N*-fluoropyridinium cation are of almost the same level, the bond distances C_2–C_3 and C_4–C_5 in **11** are short and C_3–C_4 and C_5–C_6 in **11** are long (Table 4). The former short bond distances are between a double bond (1.339 Å for CH_2=CH_2) and an aromatic bond (1.399 Å for benzene), and the latter are between the aromatic bond and a single bond (1.536 Å for CH_3–CH_3). The π-electron populations of N and C_1 in **11** are 1.560 and 0.463, respectively (Table 5). This means that the π-electron density at C_1 of **11** is greatly decreased and thus the π-orbital at C_1 is deficient in electrons as shown by the carbene form **11b**. The Mulliken charges of N (+0.194) and C_1 (−0.141) in **11** (Table 6) indicate a small polarization in the N–C_1 bonding, which is attributable to the neutral carbene form **11b**. Fig. 2 shows the lowest and the next lowest unoccupied molecular orbitals (LUMO and N-LUMO) of **11**. These orbitals are π-orbitals and the frontier electron densities at C_1 of LUMO and N-LUMO are 0.056 and 0.324, respectively (Fig. 2). The latter may thus participate in the carbene reactions. It should be noted that our RHF level calculation which does not take account of correlation effect is not sufficient to determine the energy levels of low-lying vacant orbitals.

While the *N*-fluoropyridinium cation and **11** are planar, **12** and **13** are out-of-plane, as shown in Fig. 1. According to the present calculations, a chlorine atom of chloromethane

Table 4
Calculated bond distances (Å)



	r(NF)	*r*(NC$_1$)	*r*(C$_1$C$_2$)	*r*(C$_2$C$_3$)	*r*(C$_3$C$_4$)	*r*(C$_4$C$_5$)	*r*(C$_5$N)	*r*(ClC$_1$)	*r*(ClC$_6$)
Cation [a,b]	1.320 (1.356)	1.332 (1.326)	1.376 (1.359)	1.394 (1.362)	1.394 (1.360)	1.376 (1.347)	1.332 (1.323)	–	–
11	1.352	1.314	1.440	1.364	1.422	1.351	1.359	–	–
12	1.406	1.385	1.432	1.358	1.434	1.356	1.421	1.885	1.773
13	1.437	1.457	1.439	1.356	1.437	1.355	1.441	1.657	1.975

[a] Cation; *N*-fluoropyridinium cation.
[b] Figures in parentheses are bond distances (Å) of salt **1** obtained by X-ray analysis [6].

Table 5
π-Electron populations [a]

	F	N	C_1	C_2	C_3	C_4	C_5
Cation [b]	1.960	1.507	0.837	0.978	0.783	0.978	0.837
11	1.969	1.560	0.463	1.044	0.892	1.029	0.931

[a] See Table 4 for carbon numbering.
[b] Cation; *N*-fluoropyridinium cation.

Table 6
Mulliken charges [a]

	F	N	C_1
Cation [b]	−0.155	+0.232	+0.004
11	−0.237	+0.194	−0.141

[a] See Table 4 for carbon numbering.
[b] Cation; *N*-fluoropyridinium cation.

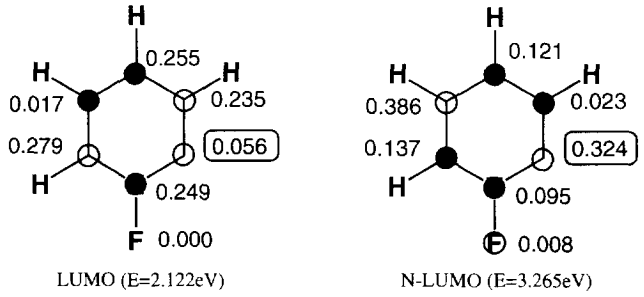
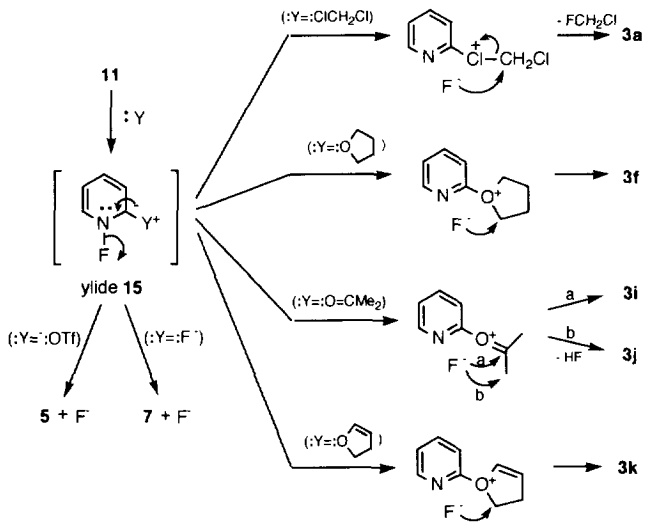
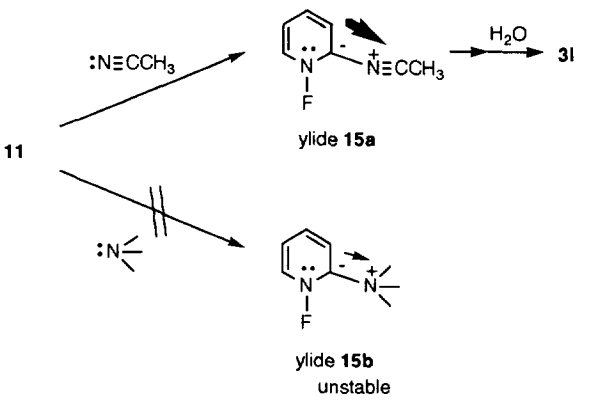


Fig. 2. The lowest and next lowest unoccupied molecular orbitals and frontier electron densities of the deprotonated *N*-fluoropyridinium cation **11**.



Scheme 3.



Scheme 4.

approaches to the π-electron-deficient C_1 carbon of **11** from the upper side of the pyridine ring and, as the reaction proceeds, the fluorine atom of N–F comes down out of the plane of the ring due to increasing repulsion with the lone-pair electrons at the nitrogen atom and the C_1 carbon. Thus, the sp^2 hybridization at the nitrogen atom of **11** changes to an almost complete sp^3 hybridization in **13**.

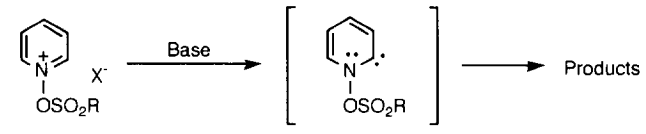
3. Discussion

It follows from the above experimental results that the reactions were initiated by bases to produce 2-substituted pyridines and the reaction rates depend on the basicity. Initiation of the reaction by even the highly hindered weak base, 2,6-di-*t*-butylpyridine, indicates that the α-protons of *N*-fluoropyridinium salts are considerably acidic. It is significant that these reactions are electrophilic in nature, as demonstrated by *O*- and *N*-attack on the carbonyl and nitrile groups in reactions with acetone and acetonitrile. Also of considerable interest is that the *N*-fluoropyridinium ring does not combine with strong nucleophiles such as diethylamine or triethylamine, as is evident from reactions using diethylamine solvent. Thus, the mechanism via the 1,2-pyridynium or 2-pyridyl cation **14** would not be applicable to these reactions, but they may be explained by the mechanism via the electrophilic singlet carbene **11** formed through α-proton abstraction from the pyridinium ring (Scheme 2).

The calculations show the deprotonated intermediate **11** as having the nature of a carbene given by the canonical formula **11b**. As seen from Table 3, the total energy change $[\Delta E = (\mathbf{14} + F^-) - \mathbf{11}]$ on going from **11** to **14** and a fluoride anion is extremely large ($+143.6$ kcal mol^{-1}), while the change $[\Delta E = \mathbf{13} - (\mathbf{11} + CH_3Cl)]$ from **11** and chloromethane to **13** is -2.1 kcal mol^{-1} and the change $[\Delta E = \mathbf{12} - (\mathbf{11} + CH_3Cl)]$ from **11** and chloromethane to the transition state **12**, which may correspond to the activation energy, is relatively small ($+18.4$ kcal mol^{-1}). Thus, intermediate **11** may experience extreme difficulty in eliminating a fluoride anion, but **11** as a carbene may react with a chlorine atom of chloromethane to form ylide **13** via transition state **12**.

Thus, the reaction mechanism for the products obtained by the present studies may be as shown in Scheme 3. The lone-pair electrons of a halogen, oxygen or nitrogen atom attack the vacant π-orbital of carbene **11** to form ylide **15**, which then reacts to give the final products through elimination of a fluoride anion. Products **3f–i** and **3k** contain their own fluorides. Acetonitrile combines with **11** to give the nitrogen-substituted pyridine **3l**, but no (alkylamino)pyridine is produced from the alkylamine. The stability of ylide **15** may possibly be the explanation for this.

It follows from Scheme 4 that ylide **15a** can be generated through the stabilization imparted by the strong electron-withdrawing effect of the $-N^+{\equiv}C-$ group, while the latter nucleophile cannot lead to ylide **15b** ($Y^+ = N^+\lessgtr$), an unstable ylide, or possibly something resembling an 8π antiaromatic ring system because of the relatively weak electron-withdrawing effect of the ammonium group. This would also perhaps explain the formation of oxygen-substituted products rather than carbon-substituted products in reactions with vinyl ethers (Runs 10 and 11 in Table 2, and Scheme 3), and the favorable formation of 2-chloro and bromo-pyridine compared to that of iodopyridine from halomethanes (Table 1 and Runs 1 and 2 in Table 2). Thus, carbene **11** reacts more easily with less reactive nucleophiles. Acetoxypyridine **3e** could never be produced by treatment with sodium acetate (Runs 9 and 10 in Table 1), while the triethylamine base-initiated reaction in trimethylsilyl acetate gave **3e** in the con-



9; R=CF3, X=OTf
16; R=Ph, X=Cl

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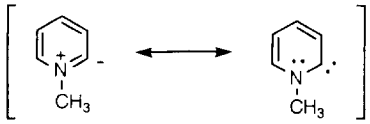
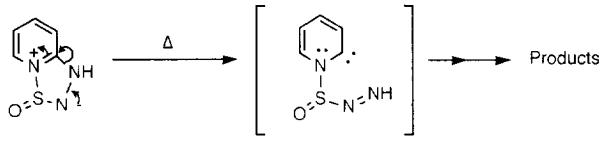
Scheme 5.



ylide form
18a

carbene form
18b

Scheme 6.



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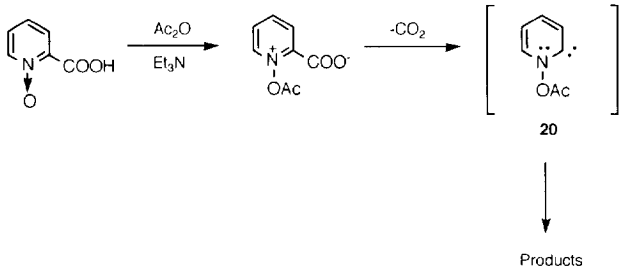
Scheme 7.



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Scheme 8.

siderable yield (Run 6 in Table 2). Sodium acetate acted only as a base. Carbene **11** is thus likely to react with the electron-deficient oxygen atom of the acetyl carbonyl group, but not with the silyl-binding oxygen atom, to give ylide **15** [$Y^+ = {}^+O{=}C(OSiMe_3)Me$] whose subsequent F^- elimination and attack on the silicon atom give **3e** and trimethylsilyl fluoride. A comparison of Run 4 with Run 5 (Table 2) readily shows that the addition of a certain amount of sodium triflate increases formation of the pyridyl triflate **5** and decreases that of methoxypyridine **3d** in spite of the large excess of methanol (solvent), thus indicating ylide **15** ($Y^+ = OTf$) to be more stable than **15** ($Y = O^+HCH_3$ or OCH_3) resulting from methanol.

The fact that **11** reacts with less reactive benzene rather than the π-electron-rich or reactive 2,3-dimethyl-2-butene may be explained by the stability of the resulting intermediate like ylide **15** as discussed above. Furan gave 1.3:1 mixture of the 2- and 3-isomers **3n** and **3o**, the explanation for which may be the same. Thus, carbene **11** would react at the less nucleophilic 3-positions of the furan ring, competing with the 2-positions.

Three other methods for preparing 2-halogenated or oxygenated pyridine derivatives are as follows: (1) reactions of pyridines with F_2 in water [8], (2) with CH_3COOF [9] and (3) with $CsSO_4F$ [10] in halogenated solvents or alcohols. Base-initiated reactions of the resulting *N*-fluoropyridinium salts underlie all these reactions. Their own counteranions, i.e. F^-, CH_3COO^- and $CsSO_4^-$ may act as such bases. Runs 9–11 in Table 1 demonstrate that CH_3COO^- and F^- act as bases for the reactions. Recently, the existence of this carbene mechanism was supported in the synthesis of pyridotriazines from *N*-fluoropyridinium salts [11].

The base-initiated reactions of salt **9** and *N*-(benzenesulfonyloxy)pyridinium chloride (**16**) may be explained by the same carbene mechanism as shown in Scheme 5. In contrast to **1** (Run 2 in Table 1), treatment of **9** in diethylamine solvent gave some base-coupled product **3p** (12%) in addition to **5** (21%). The accompanying formation of the pyridynium or pyridyl cation intermediate **14** due to the strong dissociating ability of OTf may perhaps account for this.

In sharp contrast to the above *N*-substituted pyridinium salts, *N*-cyano, -nitro, -nitroso and-(2,4-dinitrophenyl)pyridinium salts all undergo ring-opening reactions by alkaline treatment, giving glutaconaldehyde or its derivatives [12]. This mechanistic difference may possibly arise from the strong π-electron delocalizing ability of the *N*-substituents of the latter salts. Thus, the novel base-initiated reaction may be caused by *N*-substituents acting as strong σ-electron-withdrawing groups.

At this point, a comparison with the σ-electron-donating *N*-methylpyridinium salts is pertinent. Following treatment with a base, *N*-methylpyridinium salts generate the nucleophilic ylide given by the canonical formula **18a** (Scheme 6) [13]. It has also been reported that while singlet carbenes are highly electrophilic owing to vacant p-orbitals, carbenes assisted by strong electron donors become nucleophilic or take on an ylide character [14]. Pyridinium salts possessing *N*-substituents acting as strong σ-electron-withdrawing groups are shown by the present results to generate electrophilic singlet carbenes, thus indicating for the first time that *N*-substituted pyridinium salts are present in the system in which the carbene and ylide character change easily with each other due to the electronic nature of the *N*-substituents.

The thermal decomposition experiment of thiatriazole **10** afforded the same products, i.e. **3a**, **3d** and **5**, as those expected from the base-initiated reaction. Thus, this may suggest that a carbene like **19** is a reactive intermediate, as shown in Scheme 7. This is in contrast to the previous suggestion that **10** would serve as a source of the pyridynium or pyridyl cation **14** [15,16].

Quarroz has noted that when picolinic acid *N*-oxide was treated with triethylamine and acetic anhydride in dichloromethane solvent, the chloropyridine **3a** was produced [17] while the use of acetonitrile as a solvent gave (acetylamino)pyridine (**3l**) [18]. The fluorination of picolinic acid in acetonitrile has been shown here to result in the production of **3l**, thus indicating carbene **11** as being generated by the

decarboxylation of *N*-fluoropyridinium-2-carboxylate produced by fluorination at low temperature. Quarroz's results may thus be explained by the formation of carbene **20** through the decarboxylation of *N*-acetoxypyridinium-2-carboxylate as shown in Scheme 8[3].

4. Experimental details

^{1}H NMR spectra were recorded with a Varian EM 390 NMR spectrometer or a Bruker AM-400 NMR spectrometer with tetramethylsilane as internal standard. ^{19}F NMR spectra were measured with a Varian XL-300 NMR spectrometer or a Hitachi R-20B NMR spectrometer. ^{19}F NMR chemical shifts are reported in ppm upfield from trichlorofluoromethane as internal standard, unless otherwise noted. Chloroform-*d* was used as a solvent for ^{1}H and ^{19}F NMR spectral investigations. IR spectra were measured on a JASCO A-202 diffraction grating infrared spectrometer. Mass spectra were recorded on a Hitachi RMU-6MG mass spectrometer. GC analyses were carried out on an Ohkura 802 Gas Chromatograph with a column (2mm×3m) packed with PEG-6000 (15%) on Uniport B. The *N*-fluoropyridinium salts **1** and **2** were prepared according to reported methods [19]. Thiatriazole **9** was prepared by the known method [15].

Ab initio molecular orbital calculations were performed with the HONDO program (Version 8) [20] on an IBM RS/6000 computer. The calculations were done at the RHF level, and the correlated wavefunctions were not used in this work. The basis set for these calculations was of polarized double-zeta quality in the valence space on all atoms [21]. A set of diffusion functions [ζ(s) = 0.004548, ζ(p) = 0.034] was augmented for fluorine anion.

4.1. Base-initiated reactions of N-fluoropyridinium salts: Typical procedure

Into a stirred solution consisting of 1 mmol of the *N*-fluoropyridinium salt in 2 ml of dry dichloromethane was added dropwise 1 mmol of triethylamine at room temperature under an argon atmosphere. An exothermic reaction occurred immediately on adding the amine. After stirring for an additional 5 min, the reaction mixture was analyzed by GC methods. The results are listed in Tables 1 and 2. Structural assignment of the products was carried out by comparison of authentic samples or by spectral analyses of the isolated products. The spectral data and elemental analyses of new compounds are as follows:

Compound **3f:** oil. ^{1}H NMR δ: 8.14 (1H, d, J = 5.1 Hz, 6-H); 7.56 (1H, dd, J = 7.1, 8.4 Hz, 4-H); 6.85 (1H, dd, J = 5.1, 7.1 Hz, 5-H); 6.70 (1H, d, J = 8.4 Hz, 3-H); 4.51 (2H, dt, J = 47.3, 5.8 Hz, CH_2F); 4.33 (2H, t, J = 6.2 Hz, CH_2O); 1.82–1.94 [4H, m, $(CH_2)_2$] ppm. ^{19}F NMR δ: 214.7 (m) ppm. MS *m/e*: 169 (M^+). Analysis: Found: C, 63.90; H, 7.17; N, 8.35%. Calc. for $C_9H_{12}FNO$: C, 63.89; H, 7.15; N, 8.28%.

Compound **3g:** oil. ^{1}H NMR δ: 8.14 (1H, d, J = 5.2 Hz, 6-H); 7.55 (1H, dd, J = 8.4, 7.1 Hz, 4-H); 6.84 (1H, dd, J = 5.2, 7.1 Hz, 5-H); 6.72 (1H, d, J = 8.4 Hz, 3-H); 4.47 (2H, dd, J = 47.3, 6.0 Hz, CH_2F); 4.31 (2H, t, J = 6.5 Hz, OCH_2); 3.50–3.44 (4H, m, CH_2OCH_2); 1.88–1.65 [8H, m, $(CH_2)_2$×2] ppm. ^{19}F NMR δ: 218.3 (m) ppm. MS *m/e*: 241 (M^+). Analysis: Found: C, 64.99; H, 8.07; N, 6.04%. Calc. for $C_{13}H_{20}FNO_2$: C, 64.71; H, 8.35; N, 5.80%.

Compound **3h:** oil. ^{1}H NMR δ: 8.13 (1H, d, J = 5.1 Hz, 6-H); 7.55 (1H, dd, J = 7.0, 8.4 Hz, 4-H); 6.85 (1H, dd, J = 5.1, 7.0 Hz, 5-H); 6.78 (1H, d, J = 8.4 Hz, 3-H); 4.58 (2H, dt, J = 47.7, 4.2 Hz, CH_2F); 4.50 (2H, t, J = 4.8 Hz, Py-OCH_2); 3.88 (2H, t, J = 4.8 Hz, CH_2O), 3.79 (2H, dt, J = 29.5, 4.2 Hz, CH_2CH_2F) ppm. ^{19}F NMR δ: 223.1 (m) ppm. MS *m/e*:185 (M^+).

Compound **3i:** oil. ^{1}H NMR δ: 8.36–8.12 (1H, m, 6-H); 7.76–7.52 (1H, m, 4-H); 7.10–6.84 (2H, m, 3,5-H); 1.77 (6H, d, J = 17.6 Hz, CH_3×2) ppm. ^{19}F NMR δ: 90.3 (septet, J = 18 Hz) ppm. MS *m/e*: 155.075 2 (M^+) (calc. for $C_8H_{10}FNO$: 155.074 6).

Compound **3j:** oil. ^{1}H NMR δ: 8.32–8.16 (1H, m, 6-H); 7.74–7.46 (1H, m, 4-H); 7.12–6.70 (2H, m, 3,5-H); 4.68–4.38 (2H, m, $=CH_2$); 2.10–1.92 (3H, m, CH_3) ppm. IR (neat) (cm^{-1}): 1658 (C=C). MS *m/e*: 135.068 6 (M^+) (calc. for C_8H_9NO: 135.068 4).

Compound **3k:** oil. ^{1}H NMR δ: 8.19 (1H, ddd, J = 5.0, 2.0, 0.7 Hz, 6-H); 7.65 (1H, ddd, J = 8.3, 7.2, 2.0 Hz, 5-H); 7.36 (1H, dm, J = 6.3 Hz, OCH=); 6.98 (1H, ddd, J = 7.2, 5.0, 0.9 Hz, 5-H); 6.85 (1H, dm, J = 8.3 Hz, 3-H); 4.92 (1H, td, J = 7.3, 6.3 Hz, =CH–); 4.50 (1H, dt, J = 47.1, 6.6 Hz, CH_2F); 2.68 (2H, ddtd, J = 23.0, 7.3, 6.6, 1.5 Hz, CH_2CH_2F) ppm. ^{19}F NMR δ: 219.9 (tt, J = 47, 23 Hz) ppm. IR (neat) (cm^{-1}):1660 (C=C). MS *m/e*: 167.075 3 (M^+) (calc. for $C_9H_{10}FNO$: 167.074 6).

Compound **4:** oil. ^{1}H NMR δ: 8.12 (1H, d, J = 5.5 Hz, 6-H); 7.58 (1H, dd, J = 14.0, 6.3 Hz, OCH=); 7.03 (1H, dd, J = 5.5, 1.5 Hz, 5-H); 6.85 (1H, d, J = 1.5 Hz, 3-H); 4.92 (1H, dd, J = 14.0, 1.5 Hz, =CH); 4.54 (1H, dd, J = 6.3, 1.5 Hz, =CH) ppm. MS *m/e*: 177.117 9 (M^+) (calc. for $C_{11}H_{15}NO$: 177.115 2).

4.2. Base-initiated reactions of other N-substituted pyridinium salts derived from pyridine N-oxide: Typical procedure

Into a solution consisting of 95 mg of pyridine *N*-oxide (95% assay, 0.95 mmol) in 2 ml of dry dichloromethane was added 160 μl (0.95 mmol) of triflic anhydride at room temperature under an argon atmosphere. A moderately exothermic reaction occurred and a white precipitate formed from the solution. After stirring for an additional 20 min, 140 μl (1 mmol) of triethylamine was added to the reaction mixture. An exothermic reaction occurred immediately. The resulting

[3] Van Der Puy *et al.* have similarly discussed the mechanism of Quarroz's reactions on the basis of our data in their preliminary communication [8].

reaction mixture was analyzed by GC methods; the products were **3a** (29%) and **5** (34%).

4.3. Reaction of 2-picolinic acid with F_2 in acetonitrile

Following the reported fluorination method [19], a 1:9 gas mixture of F_2 and N_2 was introduced at a flow rate of 40 ml min^{-1} into a stirred solution consisting of 615 mg (5 mmol) of 2-picolinic acid in 16 ml of acetonitrile cooled at −40°C. The total amount of F_2 used was 20.6 mmol. After the reaction flask had been purged with N_2 to remove excess F_2, 6 ml of 10% hydrochloric acid was added to the reaction mixture cooled at −40°C. The mixture was warmed to room temperature and evaporated. The residue was stirred with aqueous sodium bicarbonate solution and extracted with ethyl acetate. The extract was washed with aqueous sodium chloride solution, dried with magnesium sulfate, filtered and concentrated. The residue was column-chromatographed on silica gel by using a 1:1 mixture of hexane and ethyl acetate to give 92.4 mg of **3l** (yield 14%).

4.4. Thermal decomposition of thiatriazole **10** in 1,2-dichloroethane

A solution consisting of 155 mg (1 mmol) of **10** in 2 ml of dry 1,2-dichloroethane was heated under reflux for 7 h. GC analysis of the reaction mixture showed **3a** to be formed in 17% yield.

4.5. Thermal decomposition of thiatriazole **10** in methanol in the presence of sodium triflate

A solution consisting of 159 mg (1.02 mmol) of **10** and 350 mg (2.03 mmol) of sodium triflate in 2 ml of methanol was heated under reflux for 13.5 h. GC analysis of the reaction mixture showed that **3d** and **5** were produced in 34% and 16% yield, respectively.

5. Conclusions

Novel base-initiated reactions were shown to generally occur with *N*-substituted pyridinium salts whose *N*-substituents act as strong σ-electron-withdrawing groups. The results of this study not only demonstrate new reactions for pyridinium salts, but also reveal a new, characteristic reaction species, thus extending the synthetic and mechanistic concepts of heterocyclic chemistry.

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